Remarks

Reconsideration of this Application is respectfully requested.

Claims 38-42, 45-49 and 51-57 are pending in the application, with claims 38 and 51 being the independent claims. Claims 1-37, 43, 44 and 50 are cancelled. Claims 38 and 51 have been amended. New claims 56 and 57 have been added. Support for the amendments to the claims may be found, *e.g.*, in Examples 4 and 5 of the specification. Support for new claims 56 and 57 may be found, *e.*g., in Example 6.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

Priority

At page 2 of the Office Action, the Examiner contends that Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date. First, the Examiner contends that while support for SEQ ID NO:86 has been found in Appl. No. 09/720,086 filed July 23, 2001, it is not of record in PCT/US99/14373 filed June 25, 1999 or provisional Application Nos. 60/093,993 filed July 27, 1998 and 60/090,906 filed June 25, 1998. The Examiner notes that SEQ ID NO:86 shares 99.4% sequence identity to an amino acid sequence of 912 amino acids found in Figure 2C; the drawings on page 19 of 36; and attached database sheet. The Examiner contends that Applicants are entitled to a priority date of July 23, 2001, Office Action, page 3.

At the outset, Applicants note that U.S. Appl. No. 09/720,086 is the U.S. National Stage Application of International Application No. PCT/US99/14373. Applicants also respectfully point out that July 23, 2001 is not the filing date of Appl.

No. 09/720,086, but is the date that the application met the requirements of 35 U.S.C. § 371 for entry into the U.S. National Stage, *i.e.* it is the § 371 date. This date cannot be relied upon for benefit purposes. Therefore, the filing date for U.S. Appl. No. 09/720,086 is the same as the filing date for Application No. PCT/US99/14373, *viz.*, June 25, 1999. Appl. No. 09/720,086 and Appl. No. PCT/US99/14373 are the same application and therefore the disclosures are the same. If the Examiner agrees that support for SEQ ID NO:86 has been found in Appl. No. 09/720,086, the Examiner must also necessarily agree that it is supported in Appl. No. PCT/US99/14373.

Applicants respectfully point out that the Examiner has not indicated that SEQ ID NO:85, corresponding to mouse Dnmt3a2, is not entitled to the benefit of Applicants' provisional Appl. No. 60/093,993, filed July 27, 1998 and Appl. No. 60/090,906, filed June 25, 1998. However, Applicants note that the Examiner has rejected claims encompassing SEQ ID NO:85 under 35 U.S.C. § 102 over Okano *et al.*, *infra*, which is not prior art to Applicants' provisional applications. Applicants respectfully request clarification from the Examiner.

Applicants would like to clarify for the Examiner that SEQ ID NO:86 corresponds to human DNMT3A2 polypeptide sequence and Figure 2C corresponds to the human DNMT3A polypeptide sequence (SEQ ID NO:7). Applicants are currently prosecuting claims directed to human DNMT3A sequence in Appl. No. 09/720,086. Applicants would like to clarify that both human DNMT3A and DNMT3A2 are isoforms of the same gene. The sequences are related insofar as DNMT3A2 (SEQ ID NO:86) is 100% identical to amino acids 224-912 of DNMT3A (SEQ ID NO:7). Applicants note that the nucleotide sequence of DNMT3A (SEQ ID NO:3) was amended during

prosecution of U.S. Application No. 09/720,086 to correct minor sequencing errors and Applicants relied on an ATCC deposit and nucleotide sequence disclosed in provisional Application No. 60/093,993, filed July 24, 1998, in support of the amendment. In view of the disclosure in the provisional application, the Examiner accorded Application No. 09/720,086 the benefit of the provisional application filing date for SEQ ID NO:3. Therefore, a polynucleotide encoding a polypeptide comprising amino acids 224-912 of SEQ ID NO:7 (encoded by SEQ ID NO:3), which corresponds to SEQ ID NO:86, is supported by provisional Application No. 60/093,993, filed July 24, 1998.

Rejections Under 35 U.S.C. § 112, First Paragraph (enablement)

At pages 3-5 of the Office Action, the Examiner rejected claims 38, 42 and 45-49 under 35 U.S.C. § 112, first paragraph, allegedly because the specification does not reasonably provide enablement commensurate with the scope of the claimed invention. The Examiner contends that the specification does not reasonably provide enablement for complements of the polynucleotide sequence encoding SEQ ID NOS: 85 and 86. The Examiner contends that complements listed in sections (a)-(c) of claim 38 read on fragments and not a full length polynucleotide sequence and that the complements do not read on full length complements capable of expression of full length *de novo* DNA cytosine methyltransferase polypeptides. The Examiner further contends that there is no guidance as to how to make these divergent sequences and that the products of these complements may not encode polypeptides that possess function and be commensurate with the functions of the native protein. The Examiner contends that the specification provides essentially no guidance as to what polynucleotide sequences other than those

that encode full length proteins are able to be implemented in a recombinant expression system to produce a de novo DNA cytosine methyltransferase polypeptide. The Examiner cites Lazar *et al.* as allegedly establishing that the introduction of mutations in an amino acid sequence will yield products with different biological activity from the wild type protein. Applicants respectfully traverse this rejection.

Solely to advance prosecution, and not in acquiescence of the Examiner's rejection, Applicants have amended the claims to recite that the claimed polynucleotides encode a polypeptide that methylates DNA in an *in vitro* assay. In addition, Applicants have amended part (d) of claims 38 and 51 to indicate that the complementary polynucleotide sequence is fully complementary to the polynucleotide. Applicants note that similar amendments have been made in the parent application, in reply to similar rejections by the Examiner, and that these amendments were sufficient to overcome the Examiner's rejections. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Rejection Under 35 U.S.C. § 112, First Paragraph (written description and enablement)

At pages 5-8, the Examiner rejected claims 51-55 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials. The Examiner contends that the specification lacks deposit information for the deposit of the polypeptides contained in the ATCC deposit Nos. PTA-4610 and PTA-4611 listed in claim 51. The Examiner contends that

because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed plasmids, a suitable deposit for patent purposes, evidence of public availability of the claimed plasmids or evidence of their reproducibility without undue experimentation is required. Applicants respectfully traverse this rejection.

At the outset, Applicants note the specification does in fact recite that the claimed polynucleotides were deposited at the ATCC and provides their date of deposit. Applicants direct the Examiner to the following portion of the specification:

> Clones containing mouse Dnmt3a and Dnmt3b cDNAs were deposited with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209, USA, on June 16, 1998, and assigned ATCC Deposit Nos. 209933 and 209934, respectively. The human DNMT3A cDNA was deposited with the ATCC on July 10, 1998, and assigned ATCC Deposit No. 98809. Clones containing mouse Dnmt3a2 and human DNMT3A2 were deposited with the American Type Culture Collection (ATCC) on August 23, 2002 and assigned ATCC deposit No. PTA-4611 and PTA-4610, respectively.

See paragraph [0080] of the specification, p. 26. Thus, the Examiner's requirement to submit this information at page 7 of the Office Action, last paragraph is moot.

In addition, Applicants submit herewith a Statement Concerning the Deposited Plasmids along with the filing receipt from the ATCC, an International Depository Authority, indicating that ATCC deposit Nos. PTA-4611 and PTA-4610 were submitted and accepted under the provisions of the Budapest Treaty.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Rejection Under 35 U.S.C. § 112, Second Paragraph

At pages 8-9 of the Office Action, the Examiner rejected claims 51-55 under 35 U.S.C 112, second paragraph, as allegedly indefinite because Applicants cite "mouse and human Dnmt3a2" in the Remarks, filed July 26, 2006, while claim 51 uses the acronym "Dnmt3a2" to designate the mouse form and "DNMT3A2" to designate the human form. The Examiner indicates that it is not clear which acronyms are properly identifying the claimed subject matter because of the alleged disparity presented in the Remarks and the claims language. The Examiner requests that Applicants clarify the acronyms and their corresponding SEQ ID NOS. Applicants respectfully traverse this rejection.

Applicants note that according to the specification and claims, when the acronym is in lower case letters (except for the first letter), the mouse form is intended, and when the acronym is in all capital letters, the human form is intended. Thus, SEQ ID NO:85 corresponds to mouse Dnmt3a2 polypeptide and SEQ ID NO:86 corresponds to human DNMT3A2 polypeptide. Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Rejections under 35 U.S.C. § 102

At pages 9-11 of the Office Action, the Examiner rejected claims 38, 39, 41, 42, 45-49, 51 and 53-55 under 35 U.S.C. § 102(b) as allegedly anticipated by Okano *et al.* (*Nat. Genet.* 19(3):219-220, 1998), as evidenced by Accession number AFO68625. According to the Examiner, Okano *et al.* disclose a polynucleotide sequence that is 100% and 98% sequence identical to polynucleotide sequences, which encode SEQ ID NOS:85 and 86, respectively. The Examiner also rejected claims 38, 40-42, 51, and 53-

55 under 35 U.S.C. § 102(b) as allegedly anticipated by Xie *et al.* (*Gene* 236:87-85 (1999)).[1] The Examiner also rejected claims 38, 40-42, 45-49, 51, and 53-55 under 35 U.S.C. 102(e) as allegedly anticipated by U.S. Patent Application Publication No. 2003/0083292 A1. Applicants respectfully traverse these rejections.

As described above under ***"Priority,"*** Applicants would like to clarify for the Examiner that SEQ ID NO:86 corresponds to human DNMT3A2 polypeptide sequence and corresponds to amino acids 224-912 of human DNMT3A.[2] SEQ ID NO:85 corresponds to mouse Dnmt3a2 and corresponds to amino acids 221-911 of mouse Dnmt3a.[3] Mouse Dnmt3a is fully described and supported in Applicants' provisional Appl. No. 60/090,906, filed June 25, 1998, and human DNMT3A is fully described and supported in provisional Appl. No. 60/093,993, filed July 24, 1998, the benefit of which are claimed. Thus, Applicants' provisional applications disclose polynucleotide sequences encoding a polypeptide comprising amino acids from about 1 to about 689 in SEQ ID NO:85 and from about 1 to about 689 in SEQ ID NO:86. Accordingly, none of the art cited by the Examiner is prior art to the claims.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejections.

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[1] In the Office Action, the Examiner indicated that Xie *et al.* was published in 1995, however, this is a typographical error.

[2] The nucleotide sequence of human DNMT3A is represented by SEQ ID NO:3 and the polypeptide sequence is represented by SEQ ID NO:7.

[3] The nucleotide sequence of mouse Dnmt3a is represented by SEQ ID NO:1 and the polypeptide sequence is represented by SEQ ID NO:5.

Rejections under 35 U.S.C. § 103

The Examiner rejected claims 38, 40-42 and 45-49 under 35 U.S.C. § 103 as allegedly obvious over Xie *et al.* in view of Okano *et al.* The Examiner alleged that while Xie *et al.* does not teach the disclosed polynucleotide inserted in a recombinant vector and host cell and the method for producing a *de novo* DNA cytosine methyltransferase polypeptide by the means presented in claims 45-49, Okano *et al.* teaches the *de novo* DNA cytosine methyltransferase polypeptide transcripts expressed in embryonic stem cells (ES) using baculovirus expression vectors and their ability to methylate DNA substrates. Applicants respectfully traverse this rejection.

As described above, neither Okano *et al.* nor Xie *et al.* is prior art to Applicants' claims. Therefore, whether or not there would be proper motivation to combine the alleged teachings of the cited art is not material. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned directly at (202) 772-8658.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

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